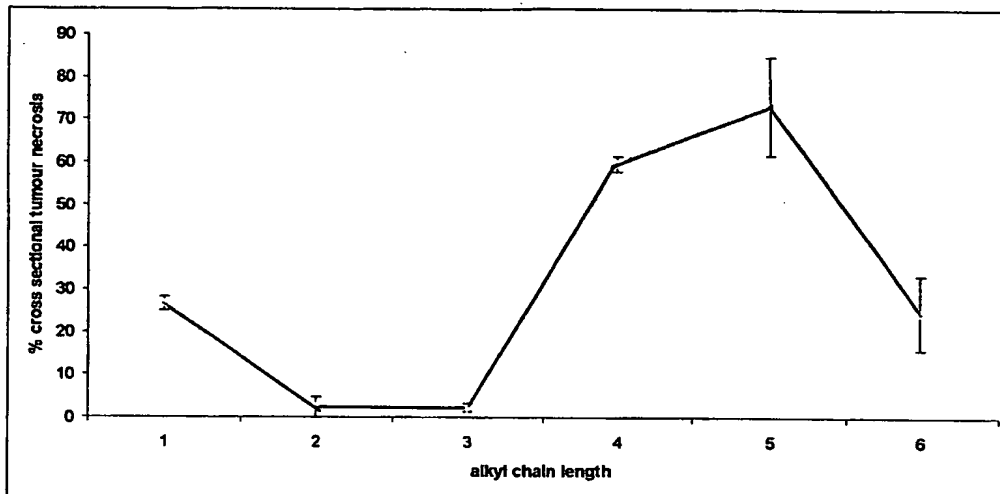


**Figure 1****Symmetrical phenothiazinium salts: *in vivo* activity at 1h**

Figure shows % cross sectional tumour necrosis at 72h post-PDT. All drugs were administered i.v. at a dose of  $16.7\mu\text{mol/kg}$ . At 1h post drug administration light ( $60\text{J/cm}^2$ ,  $50\text{mW/cm}^2$ ) was administered superficially.



Symmetrical phenothiazinium salt	Alkyl chain length	Vehicle	Wavelength (nm $\pm$ 15)	%area	s.e.m
Methyl	1	Phys. saline	685	26.70	1.60
Ethyl	2	Phys. saline	630	2.38	2.38
Propyl	3	2%DMSO/H <sub>2</sub> O	630	2.27	0.99
Butyl	4	2%DMSO/H <sub>2</sub> O	660	59.74	1.78
Pentyl	5	2%DMSO/H <sub>2</sub> O	685	73.31	11.57
Hexyl	6	2%DMSO/H <sub>2</sub> O	660	24.71	8.74

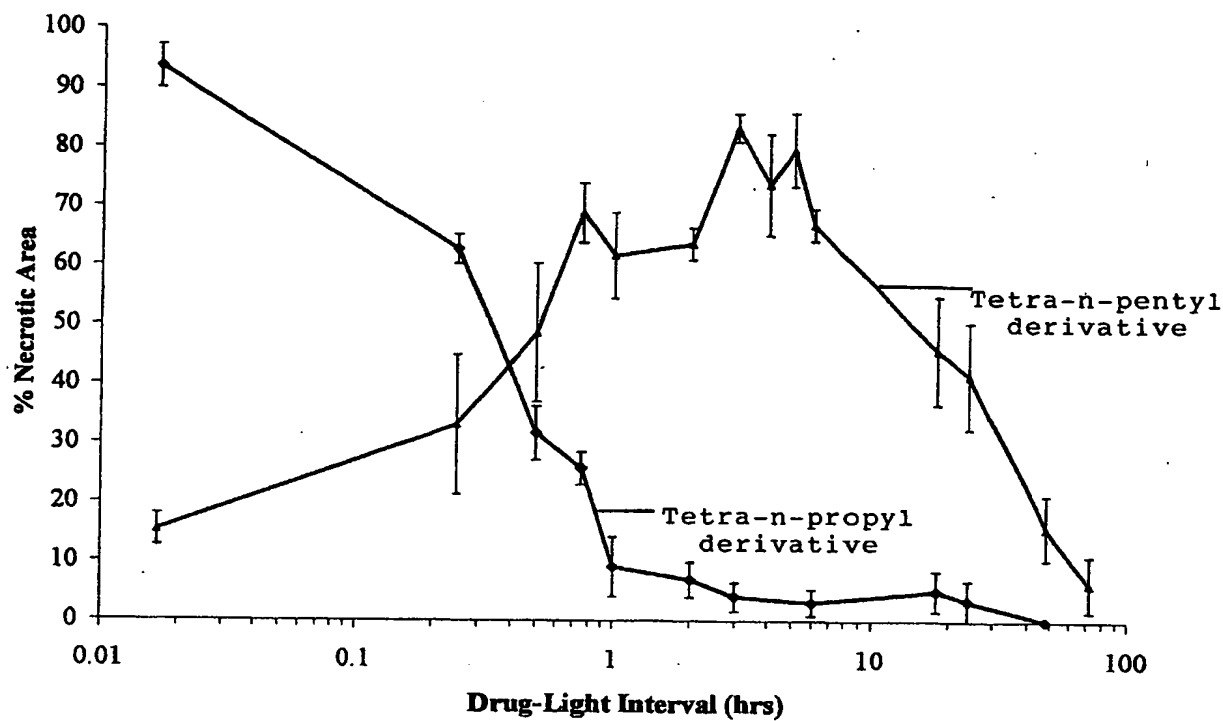


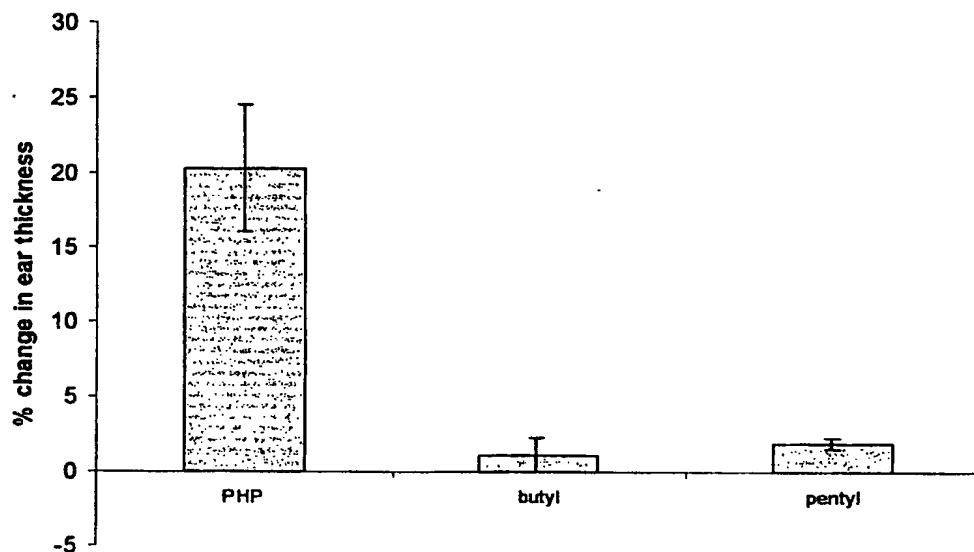
Figure 2: Area of tumour necrosis (expressed as a % total section area) 72 hrs after PDT with tetra-n-propyl and tetra-n-pentyl derivative ( $16.7\mu\text{molkg}^{-1}$ , 660nm light @  $50\text{mWcm}^{-2}$ ,  $60\text{Jcm}^{-2}$ ). Data points represent mean + SEM (n=6, each reading measured in triplicate).

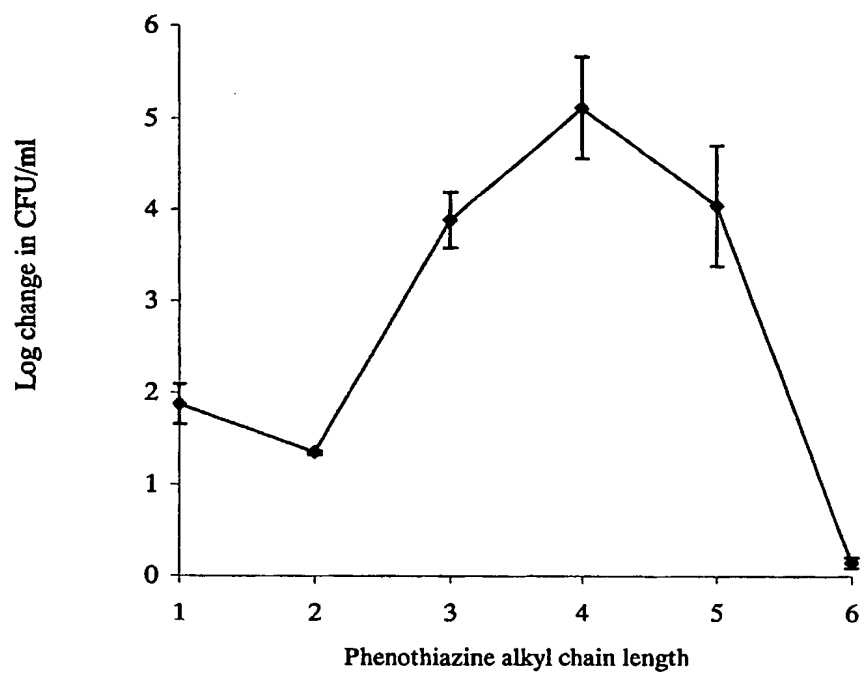
**Figure 3****Skin photosensitivity- murine ear swelling response**

CBA/Gy mice were injected with sensitiser at 16.7  $\mu\text{mol/kg}$ . At 24h post drug injection ears were exposed to broad band white light from a xenon arc lamp ( $25\text{J}/\text{cm}^2$ ,  $30\text{mW}/\text{cm}^2$ ). % Change in ear thickness was measured as :

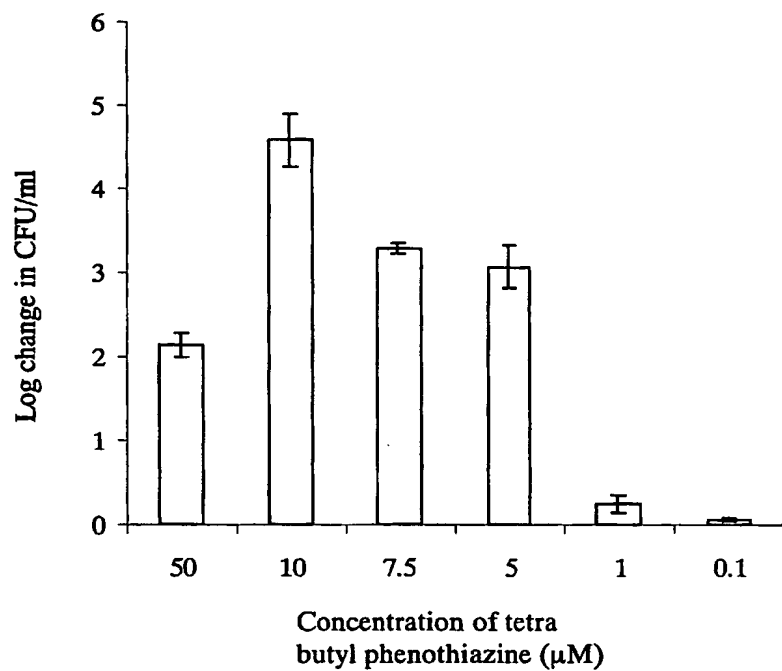
$$\frac{(\text{ear thickness at 24h post illumination} - \text{ear thickness pre-illumination})}{\text{ear thickness pre-illumination}} \times 100$$

Increased % change in ear thickness measures increased skin photosensitivity.

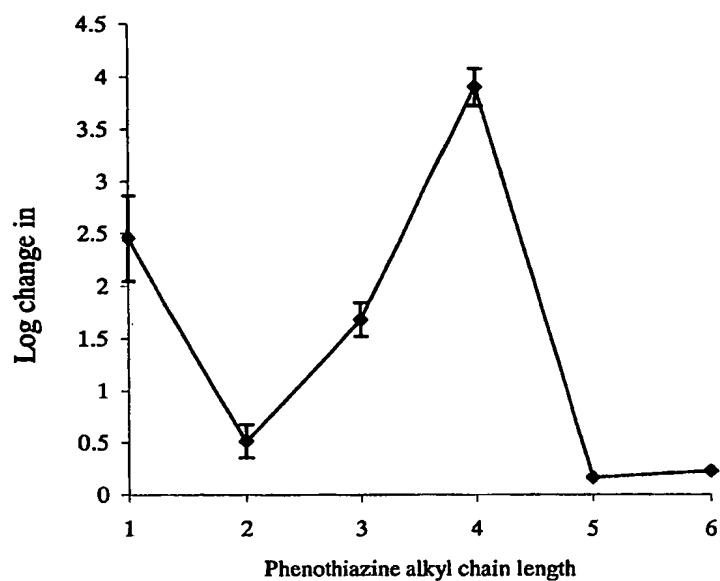




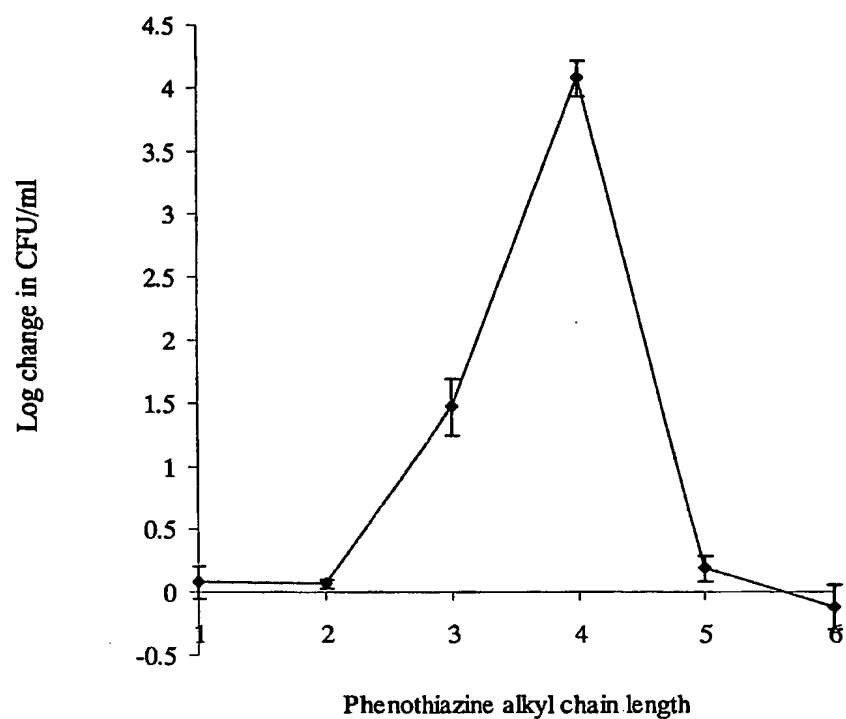
**Figure 4** Log change in CFU/ml of *E.coli* incubated for 30 minutes with 10 $\mu$ M phenothiazine and illuminated for 60 minutes at 1.3mW/cm<sup>2</sup>



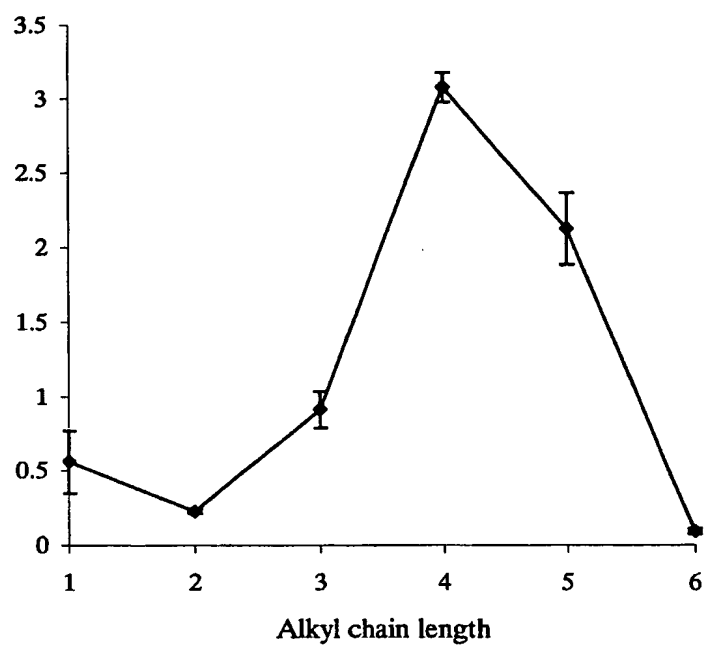
**Figure 5** Log change in CFU/ml of *E.coli* incubated for 30 minutes with different concentrations of tetra butyl phenothiazine and illuminated for 15 minutes at  $1.3\text{mW/cm}^2$



**Figure 6 Log change in CFU/ml of *E. coli* in the stationary phase of growth following incubation for 30 minutes with 10  $\mu$ M phenothiazine and illuminated for 60 minutes at 1.3 mW cm<sup>-2</sup>**

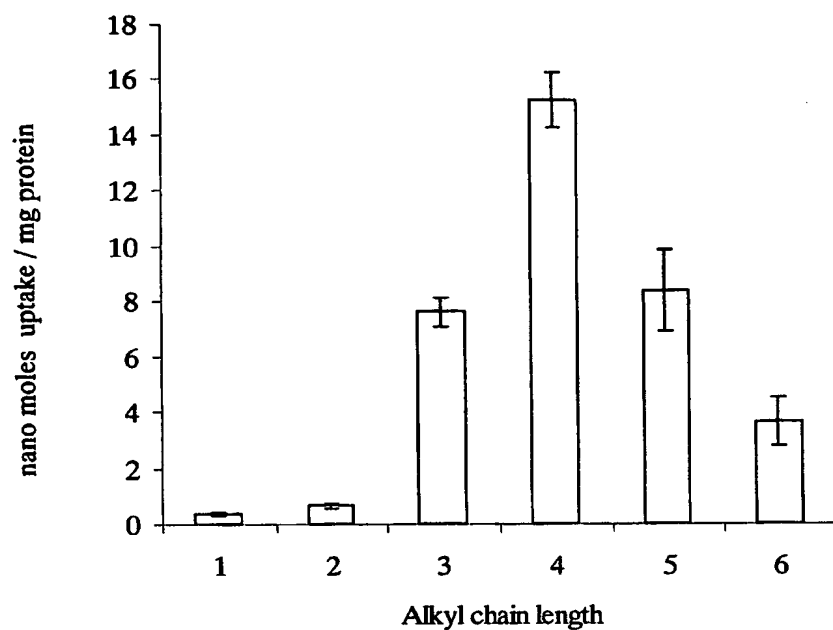


**Figure 7 Log change in CFU/ml of *E.coli* resuspended in nutrient media. Cells were incubated for 30 minutes with 10 $\mu$ M phenothiazine and illuminated for 60 minutes at 1.3mW/cm<sup>2</sup>**

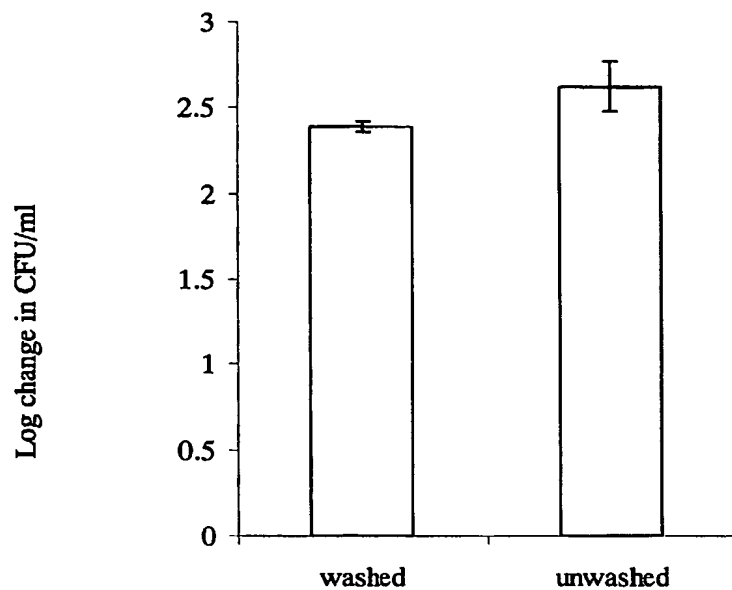


**Figure 8 Log change in CFU/ml of *E.coli* following incubation with 10  $\mu$ M phenothiazine for 30 minutes. Illumination was with laser light (664nm) for 4 minutes at 0.1W**

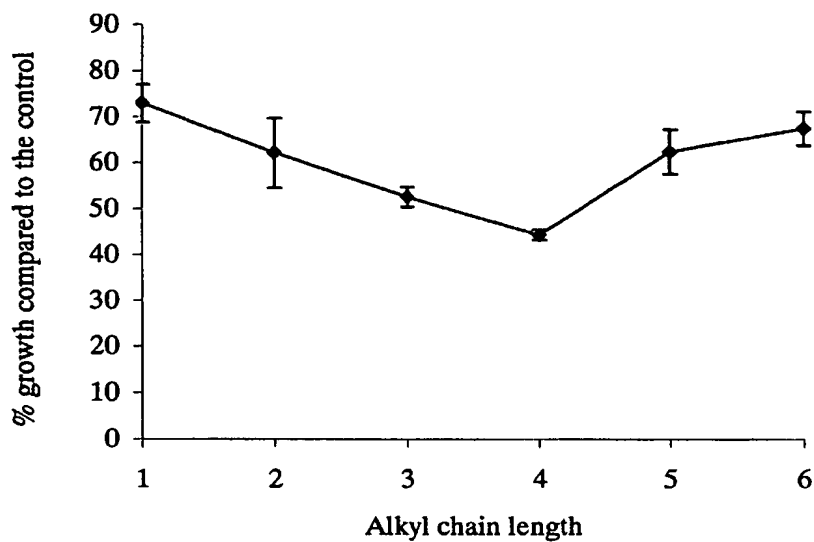




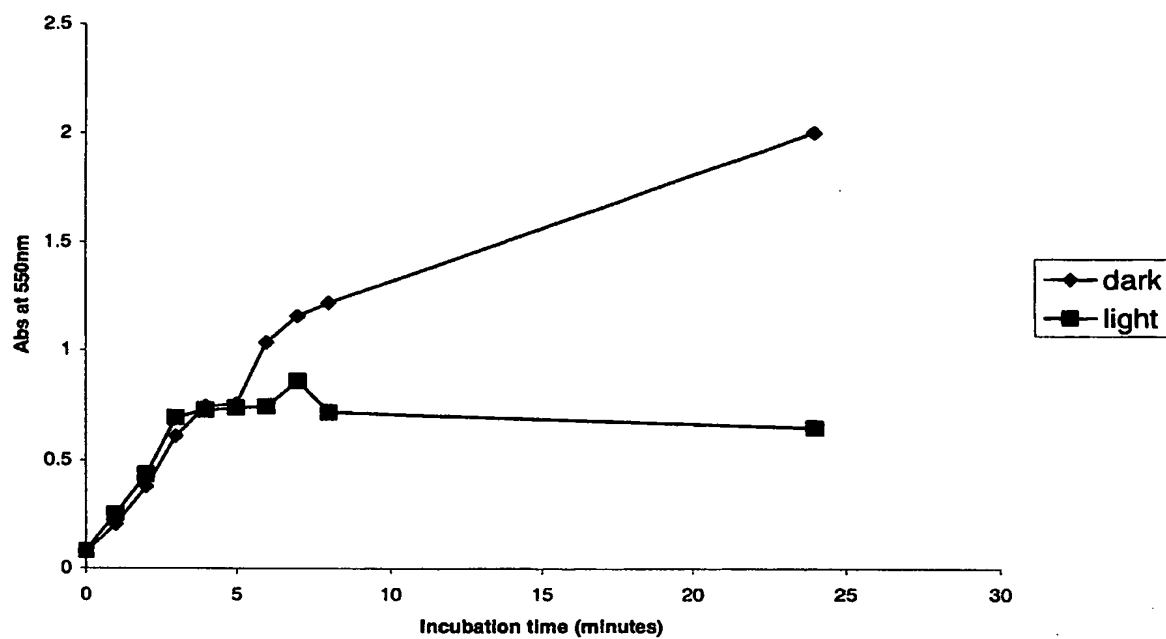
**Figure 9 Uptake of 10µM phenothiazine into *E.coli* cells following a 30 minute incubation. Cells were washed twice in 0.1M pH7.0 potassium phosphate buffer to remove extra-cellular or loosely bound sensitiser.**



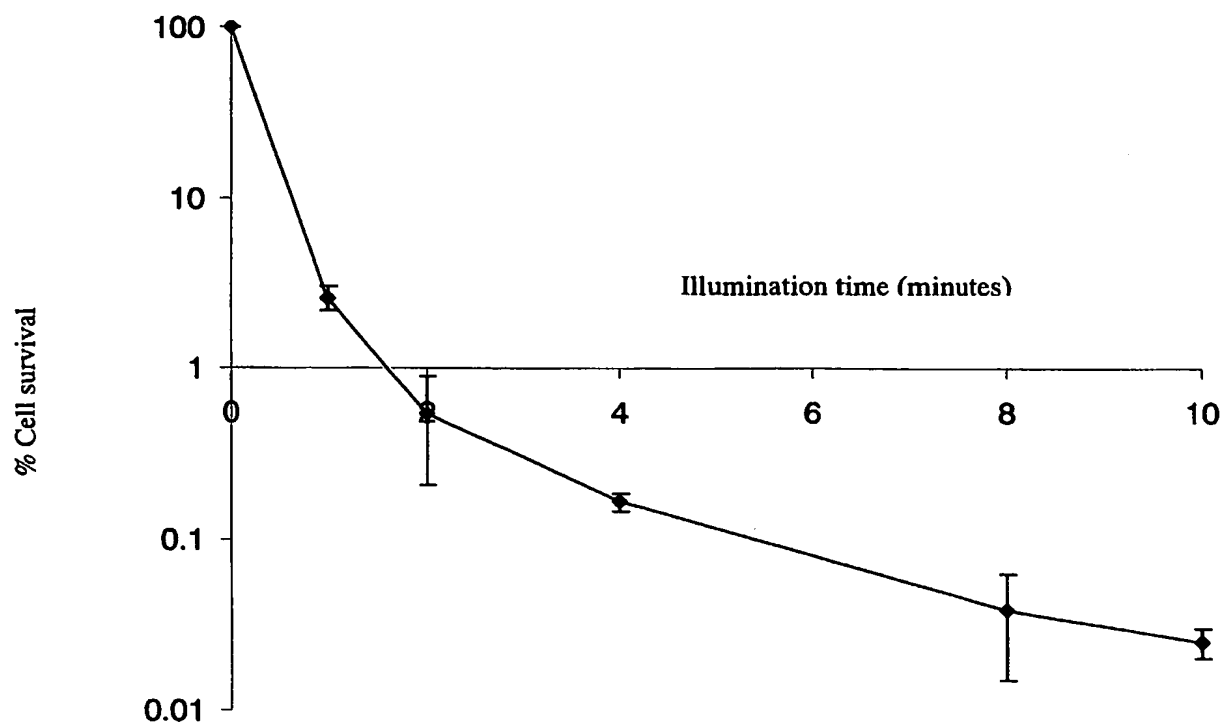
**Figure 10** Log change in CFU/ml of *E.coli* cells incubated with 10 $\mu$ M tetra butyl phenothiazine. Cells were washed twice with 0.1M pH7 potassium phosphate buffer. Illumination used laser light (664nm) at 0.1W for 4 minutes.



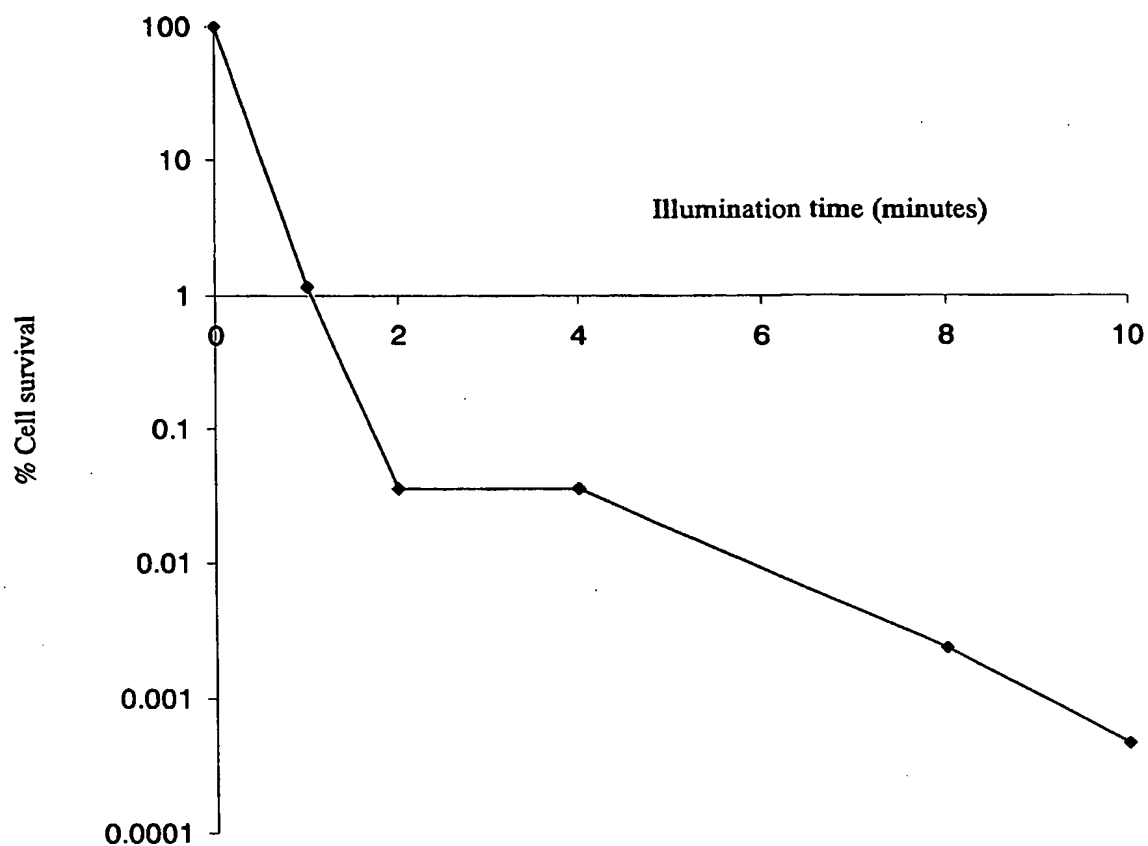
**Figure 11 Percentage growth of a culture of an *E. coli* culture as compared to a control when 10 $\mu$ M phenothiazine was included in the growth media. Incubation was carried out in the dark at 37°C for 6 hours. Measurements based on apparent turbidity at 550nm.**



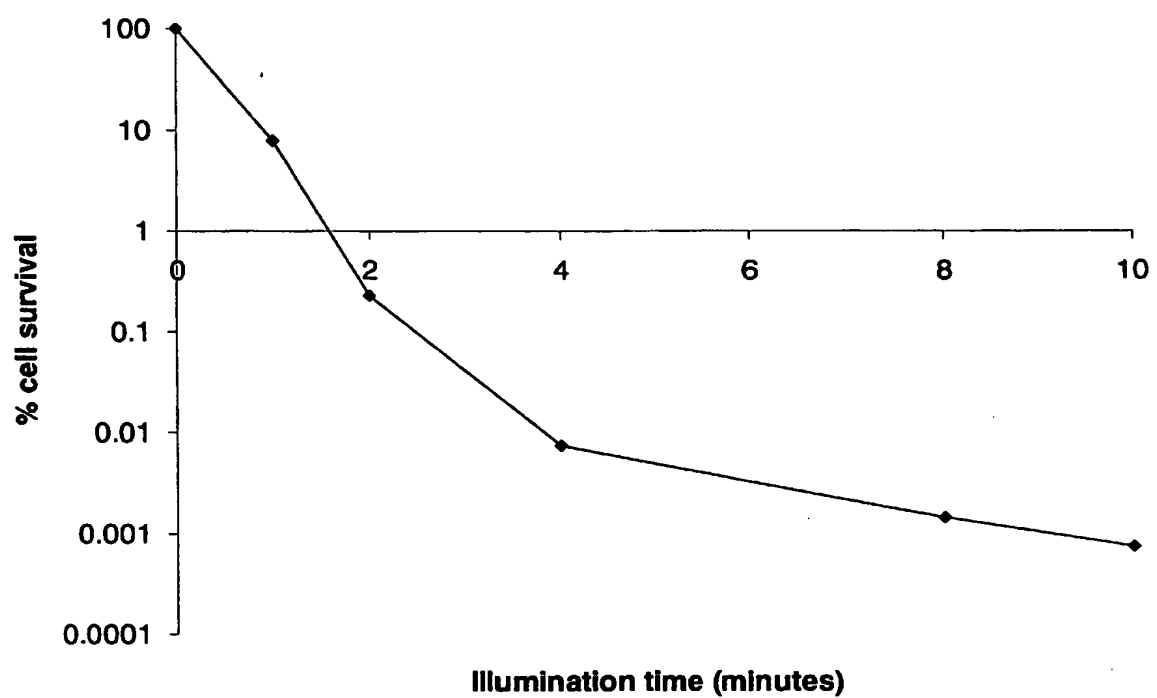
**Figure 12** Change in absorbance of an *E.coli* culture grown in the presence of 10 $\mu$ M tetra butyl phenothiazine in the light and in the dark



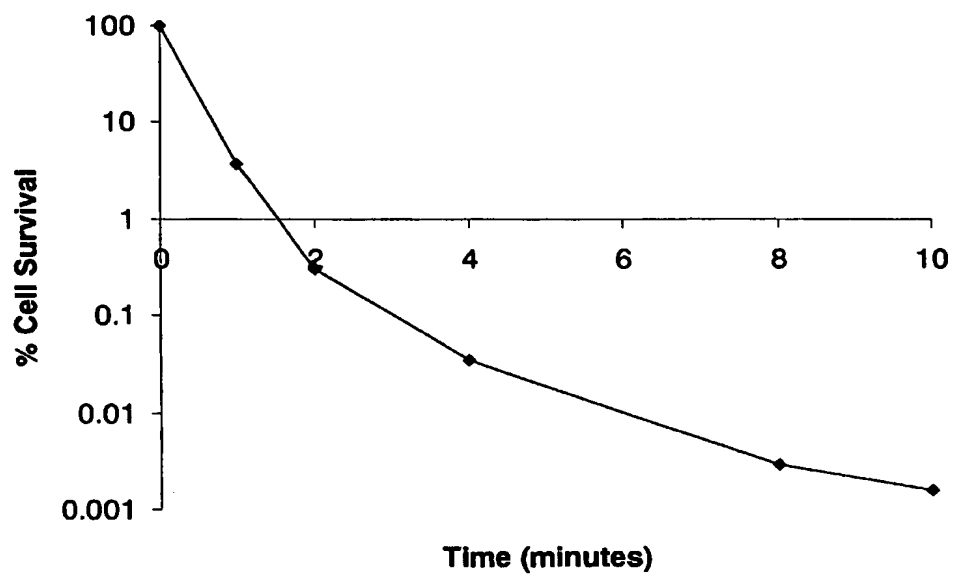
**Figure 13 Percentage cell survival of *P.aeruginosa* following incubation with 10 $\mu$ M tetra butyl phenothiazine. Illumination was with laser light (664nm) at 0.1 W.**



**Figure 14 Percentage cell survival of *S. aureus* following incubation with 10 $\mu$ M tetra butyl phenothiazine. Illumination was with laser light (664nm) at 0.1 W.**



**Figure 15 Percentage cell survival of MRSA following incubation with 10 $\mu$ M tetra butyl phenothiazine. Illumination was with laser light (664nm) at 0.1W**



**Figure 16 Percentage cell survival of *C.albicans* following incubation with 10 $\mu$ M tetra butyl phenothiazine. Illumination was with laser light (664nm) at 0.1W**



Figure 17

Protocol:

Drug applied topically, dose = 5.79  $\mu\text{g}$  (20 $\mu\text{l}$  at 0.5mM)Applied light dose = 25J/cm<sup>2</sup> (30mW/cm<sup>2</sup> for 831sec)

1	PHP (i.v.) 8.35 $\mu\text{mol/kg}$ 24h drug to light interval (solar simulator)
2	PHP (i.v.) 8.35 $\mu\text{mol/kg}$ 2wk drug to light interval (solar simulator)
3	Butyl phenothiazinium drug only for 30min
4	24h ROOM LIGHT + Butyl phenothiazinium
5	24h ROOM LIGHT
6	24h DARK + Butyl phenothiazinium
7	24h DARK
8	Butyl phenothiazinium 30min drug to light interval (660 $\pm$ 15nm)
9	Butyl phenothiazinium 30min drug to light interval (solar simulator)
10	Butyl phenothiazinium 24h drug to light interval (solar simulator)
11	Butyl phenothiazinium 7 days drug to light interval (solar simulator)
12	Butyl phenothiazinium 14 days drug to light interval (solar simulator)

